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Richard T. James Jr. M.D.

Editor/Publisher.

10-1 A TWO-DECADE COMPARISON OF PREVALENCE OF DEMENTIA IN INDIVIDUALS AGE 65 AND OLDER FROM THREE GEOGRAPHICAL AREAS OF ENGLAND: The Cognitive Function and Aging Study (CFAS I and CFAS II)

The prevalence of dementia is of interest worldwide. Contemporary estimates are needed to plan for future care.

This study investigated whether the prevalence of dementia has changed in the past 2 decades by using the same approach and diagnostic methods used in the Medical Research Council Cognitive Function and Aging Study (CFAS) in 3 of the original study areas in England.

STUDY

1. Between 1985 and 1994 (CFAS I) conducted baseline interviews in populations age 65 and older in 3 geographically defined areas in England (Cambridgeshire, Newcastle, and Nottingham) to estimate dementia prevalence.
2. Between 2008 and 2011, a new study (CFAS II) was done in the areas.
3. Both studies used identical sampling approach and diagnostic methods.
4. Each area included 2500 individuals age 65 and older to provide power for geographical and generational comparison.

RESULTS

1. In CFAS I, 7635 people age 65 and older responded (80% response). In CFAS II, 7796 responded (56% response).
2. Using CFAS I age and sex specific estimates of prevalence of dementia standardized to the 2011 population, 8.3% of this population would be expected to have dementia. However, CFAS II shows that the prevalence was actually 6.5%. (a decrease of 1.8%; odds ratio = 0.7)
3. Prevalence of dementia increased with age in CFAS II as well as in CFA I, but at a slower rate, For each 5-year age group, the prevalence of dementia was consistently lower in CFAS II than in CFAS I.

DISCUSSION

1. This study provides compelling evidence of a reduction in prevalence of dementia in the older population over 2 decades.

2. On the basis of age and sex specific estimates from CFAS I, 66 400 individuals were estimated to have dementia in 1991. Taking into account only the effects of population aging, this number would be expected to be 884 000. However, the results of CFAS II suggest that the number of people with dementia in 2011 was 670 000—214 000 fewer than population aging alone would have predicted (reduction of 24%).
3. Prevalence varies according to deprivation indices. There is substantial variation in expected prevalence of dementia across England.
4. Prevalence of dementia patients has increased in care settings.
5. Whether or not these gains identified for the present older population will be borne out in later generations will probably depend on achievement of further improvements in primary prevention and effective health care for disorders that increase risk of dementia.

CONCLUSION

This study provides further evidence that a cohort effect exists in dementia prevalence. Later-born populations have a lower risk of prevalent dementia.

Lancet October 26, 2011; 382:1405-12 Original investigation, first author Fiona E Matthews,
 Funded by the UK Medical Research Council

I believe that healthy lifestyles can reduce risk of vascular dementia. But Alzheimer's disease has an entirely different pathogenesis. We await evidence on prevention of Alzheimer's.

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“What is good for your heart is good for your head”

10-2 GOOD NEWS ON DEMENTIA PREVALENCE—WE CAN MAKE A DIFFERENCE:

Comment

The findings of the preceding study are unequivocally good news. The study suggests that the prevalence of dementia in three areas of England in 2011 (CFAS II) was significantly lower than would have been expected based on the estimated prevalence in 1991 (CFAS I).

The age and sex specific prevalence estimates from CFAS I, indicated that 66 400 individuals were estimated to have dementia in 1991. After applying the effects of population aging to this estimate, the number of people with dementia was projected to be 88 400 in 2011. However, the results CFAS II suggests that the number of people with dementia in 2011 was 67 000, a decrease in a prevalence from 8.3% in 1991 to 6.5% in 2011. (Odds ratio = 0.70)

As with any research criteria, the diagnostic system used in this study has limitation. The low response rate might be a source of error. Even with adjustments, it remains entirely possible that there was substantial response bias, which might have a substantive effect on the prevalence estimates.

However, the data do suggest that things the population has done have decreased the age-specific incidence of dementia, and the number of people with dementia is lower than it would have been without making these changes. The adage“ What is good for your heart is good for your head” seems to be supported by this new evidence.

It is plausible that changes in health behavior including smoking cessation, and improved management of cardiovascular risk factors have prevented or delayed onset of dementia at the population level. The next question must be: how much further can we go in pursuit of the preventive agenda? How many more cases can be prevented? What do we need to do? These questions need empirical investigation.

A powerful message from the data is that what individuals and services do matters in terms of dementia. The data point to substantial added value from existing healthy lifestyles. Change in diet, exercise, and smoking might reduce risk of dementia and promote general health and well being. Inclusion of the potential benefits of dementia prevention in communications could drive greater adoption of healthy lifestyles with resulting benefits for individuals and society.

But there is a need for caution in predicting future numbers with dementia. If positive changes in health behavior can decrease prevalence of dementia, then negative lifestyle changes might promote dementia. It is possible that the present epidemic of obesity, with consequent cardiovascular disorders, stroke, and diabetes might act to increase dementia in future cohorts. If positive changes in lifestyle can decrease prevalence of dementia, then negative lifestyles might promote it.

Even with the positive changes in risk, dementia remains common, very expensive, and profoundly negative in its effect on patients and their families.

Dementia remains one of the greatest challenges faced by health care and social-care systems worldwide. It has macroeconomic effects. At least three quarters of people now in care homes in the UK have dementia.

Dementia is a powerful example of the complexity and long-term nature of the disorders that are now outstanding challenges for healthcare systems. The great majority of patients with dementia also has other long-term disorders.

The results of the CFAS study suggest that prevention is possible. The findings should spur us on to go further and faster in prevention of dementia. This study shows that we can make a difference.

Lancet October 26, 2013;382: 1384-86 “Comment” by Sube Bonerjee, University of Sussex, Brighton, UK

Patients who maintain a healthy lifestyle to prevent diabetes, heart disease and obesity may now add another benefit—preventing of dementia.

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Hope for the “Silent Epidemic”

10-3 NEW INSIGHTS INTO THE DEMENTIA EPIDEMIC: Comment

Described in the 1980s as “The Silent Epidemic”, dementia in the elderly will soon become a clarion cry for public health experts worldwide.

In most countries around the world, especially wealthy ones, the “old old” population will continue to grow, and since it accounts for the largest portion of dementia cases, the dementia epidemic will grow. The combined effects of longer life and the dramatic bulge of baby boomers reaching old age will magnify the epidemic in future decades.

However, recent reports point to declining age-specific prevalence of dementia among people born later in the first half of the 20th century.

These reports are intriguing and inform our understanding of potentially modifiable factors that contribute to the epidemic. Knowing about the contributing factors is especially important for development of preventive strategies.

In 2005, an intriguing article¹ was published analyzing 17 years (1982-99) of national long-term surveys. It reported a decrease in dementia from 5.7% to 2.9%. It pointed to higher levels of education, and a reduction in stroke rates as contributing to the decrease.

The US Health And Retirement Study,² is an ongoing population-based longitudinal survey of nationally representative samples of older adults. In 1993, 12.2% of surveyed adults age 70 and older had cognitive impairment compared with 8.7% in 2002. The results suggested that overall the combined impact of recent trends in educational, lifestyle, demographic and social factors had a positive effect

The Rotterdam Study (1990-2000)³ studied a cohort of persons age 55 and older. Incidence of dementia was lower in 2000. Most intriguing was the observation of larger brain volumes and less extensive small-vessel disease on MRI imaging in persons born later. The authors hypothesized that these changes were attributable to secular changes in education, population-level reductions in vascular risk factors, and an overall reduction in stroke.

A Swedish study (2013)⁴ entered 2 cross-sectional surveys of people age 75 and older (in 1987-88 and 2001-2004). The age and sex-standardized prevalence of dementia was similar in both surveys (17.4% and 17.9%). However, because the hazard ratio for death was lower in the later cohort, including persons with dementia, the authors argued that the incidence of dementia may have decreased, probably due to favorable changes in vascular risk factors and healthier lifestyles, especially among older people.

The most recent study from the UK (abstracted below) also reported declines in dementia over time.

The consistency of the findings is encouraging, especially since the projected growth of the population older than age 75 guarantees a growth in the epidemic of dementia. For now, the evidence supports the theory that better education (use it or lose it) and greater economic well-being enhances life expectancy and reduces the risk of dementia. The results also suggest that controlling vascular and other risk factors during midlife and early old age have unexpected benefits.

These studies illustrate the potential for deriving widespread public health benefits from improving educational opportunities in both early and later life, reducing cardiovascular risk factors, and promoting greater physical activity.

The studies also remind us that dementia is a syndrome with multiple causes.

Population-based studies have convincingly demonstrated that the vast majority of dementia cases, especially those occurring very late in life, tend to involve a mixture of Alzheimer's disease, cardiovascular disease and other degenerative factors.

However, a potentially ominous trend that could lead to a reversal of the decrease in risk is the growing prevalence of obesity and diabetes among the young and middle-aged. Improvement in life-expectancy will certainly lead to an increase in the number of people with dementia later in life. This justifies the value of learning more about lifestyle and risk factors that affect dementia rates.

Research to uncover influences on these trends has great promise.

NEJM December 12, 2013;369: 2275-77 “Perspective”, first author Eric B Larson, University of Washington, Seattle

I believe that primary care clinicians may now advise patients that healthy lifestyles, continuing mental activity, and interventions to reduce risk factors for vascular disease will delay onset of dementia.

We can reduce prevalence of vascular dementia, although continuing studies are required to strengthen the evidence.

There seems to be a race between A) benefits of lifestyles, which delay onset of dementia and B) increasing longevity, which will increase prevalence of dementia.

We need continuing studies on this massive public health problem, especially for Alzheimer’s disease.

Can dementia in the very, very old be prevented?

1. Adv Gerontol 2005;16:30-37 First author K C Marton
2. Alzheimers Dementia 2008;4:134-44 First author K M Langa
3. Neurology 2012;78:1456-63 First author EMC Schrivvers
4. Neurology 2013;80:1888-94 First author C Qiu
5. See abstract from Lancet below.

10-4 BETTER DIET QUALITY AND DECREASED MORTALITY AMONG MYOCARDIAL INFARCTION SURVIVORS: Original investigation

Patients with coronary heart disease have a substantially shorter life expectancy.

Life style changes in MI survivors (smoking cessation, regular physical activity and diet improvements) may reduce mortality. In the US, approximately 80 000 lives per year could be saved through optimizing secondary prevention strategies.

Despite these potential benefits, patients often report poor diet quality after MI.

The traditional low-fat diet has failed to improve cardiovascular risk profiles and MI prognosis.

The Alternative Healthy Eating Index 2010 (AHEI2010) is based on a comprehensive review of foods most consistently associated with chronic disease risk. In the general population, a higher AHEI2010 score is associated with a 23% lower risk of cardiovascular disease. The index includes 11 components. Some are healthful: vegetables, fruits, nuts and legumes, polyunsaturated fats, omega-3 fats, whole grains. Some are harmful: processed meats, sugar-sweetened beverages, trans fats, and high salt intake. Alcohol is both, moderate drinking is healthful; binge drinking is harmful.

At an advanced stage of the atherosclerotic process, whether, and to what degree, dietary changes from pre- to post-MI improve prognosis is not clear.

This study examined changes in the post-MI AHEI2010 diet and their effect on all-cause mortality and cardiovascular mortality.

STUDY

1. The Nurses' Health Study (NHS; n = 121 700) is a large prospective cohort study of female nurses age 30-55 at baseline. The Health Professionals Follow-up Study (HPFS; n = 51 529) is a large prospective cohort study of US male health professionals age 40-75 at baseline.
2. Included 2258 women and 1840 men who were free of cardiovascular disease at enrollment and survived a first MI during follow-up. All provided pre-MI and post-MI food frequency questionnaire (FFQ).
3. Diet was assessed every 4 years using a FFQ.
4. Diet quality was measured using the AHEI2010 score to determine scores for food and nutrients most commonly associated with chronic disease. The score for each of the 11 components ranged from 0 (worst) to 10 (best) and the total AHEI2010 score ranging from 0 (minimal adherence) to 110 (maximum adherence).
5. Divided the cohorts into 5 groups (quintiles)—least healthy to most healthy diet depending on AHEI2010 score.
6. Outcomes were all-cause mortality and cardiovascular mortality.

RESULTS

1. Follow-up included 502 all-cause deaths (232 cardiovascular) in women; in men, 451 and 222. The median survival time after MI onset was 8.7 years for women and 9.0 for men.
2. Participants on average improved dietary quality from pre- to post-MI, with an increase in AHEI2010 score in men (median change 5.5) than for women (2.1).
3. Multivariate-adjusted changes in mortality according to change in AHEI2-10 score from pre-MI to post-MI (Adjusted hazard ratios according to degree of change.)

1) All cause mortality	Q1 (least change)	Q5 (most change)
A. Women (n = 502)		
Number of deaths	133	78
Person-years	3368	3334
Changes in score	-10	+17
Median range		+12 to +49
HR	1.00	0.63
B. Men (N = 451)		
Number of deaths	114	62
Person-years	3202	3242
Changes in score	-8	+18
Median range		+13 to 56
HR	1.00	0.81*
Pooled HR	1.00	0.71
2) Cardiovascular mortality		
A. Women (n = 232)		
Number of deaths	59	32
Person-years	3368	3334
Changes in score	-10	+17
Median range		+12 to +49
HR	1.00	0.55

B. Men (n = 222)

Number of deaths	56	30
Person-years	3202	3242
Changes in	-8	+18
Median range		+13 to +56
HR	1.00	0.65*
Pooled HR for CVD death		
(Woman and men)	1.00	0.60

(*not statistically significant)

4. For both men and women, the greatest improvement in dietary quality from pre- to post-MI was an increase in whole grain intake and a reduction in consumption of trans fat and red and processed meat.
5. Post-MI diet quality and prognosis: Comparing the highest vs lowest quartiles, the AHEI2010 score was highly significantly associated with low all-cause mortality in women but not in men. Those in the fifth quintile of AHEI2010 had a better prognosis compared with the first quintile for both men and women.

DISCUSSION

1. Comparing extreme quintiles (multivariate-adjusted and pooled for both women and men), the highest AHEI2010 score post-MI was associated with a 29% lower all-cause mortality and a 40% lower cardiovascular mortality,
2. Sugar-sweetened fruit juice and beverages had the lowest component score on the post-MI diet.
4. Post-MI, patients also reduced saturated fat, trans fat and polyunsaturated fat.
5. The Mediterranean diet (MD) has also been reported to reduce cardiovascular death among MI survivors.
6. The stronger association of the AHEI2010 score with mortality than the associations for individual components suggests that the diet captures the synergistic or interactive effects of dietary components.
7. The development of atherosclerotic disease is complicated, and has origins in lipids, inflammation, coagulation, and endothelial activity. Although not all mechanisms are understood, it is likely that many of the underlying biological pathways are similar in the pre-and post-MI periods.
8. The association between the post-MI diet quality, and changes from pre- to post MI with mortality,

were stronger for women than for men. This differs from previous studies of diet for primary prevention. Further studies are needed to clarify this point.

9. Moderate alcohol intake is an important contributor to the AHEI2010 score and is associated with lower all-cause and cardiovascular mortality.
10. This study was conducted in cohorts of health professionals. Results may not be generalizable to all post-Mi patients.

CONCLUSION

These results suggest that post-MI patients who consume a higher quality diet have lower all-cause mortality.

Greater improvements from the pre- to post-MI are strongly associated with lower all-cause mortality and cardiovascular mortality .

JAMA Internal Medicine October 28, 2013;173:1808-20 Original investigation, first author Shanshan LI, Harvard School of Public Health, Boston Mass

I found this a complex and difficult-to abstract article. I congratulate the investigators on their ability to dig through mountains of data.

The sophisticated health care professionals made little changes in their post-MI. Diet improvements were small.

Many MI survivors were taking other preventive measures—statins, ACE inhibitors, beta-blockers, anti-platelets, and cardiac rehabilitation.

A healthy diet is an important application for both primary and secondary care. It is never too late to start a healthy diet. Benefits may be evident within a few years.

Primary care clinicians should emphasize diet along with smoking cessation, BP and weight control, and continued physical activity.

In select patients, moderate alcohol consumption (a glass of wine with dinner) will reduce incidence of atherosclerosis.

The AHEI2010 diet does not differ greatly from the Mediterranean diet and the USDA Food Pyramid.

PAD is preventable

10-5 THE GLOBAL PANDEMIC OF PERIPHERAL ARTERIAL DISEASE: Comment

The global burden of non-communicable disease (N-CD) greatly impairs community health. Yet, we have not created a fully accurate description of N-CD. When individuals are unable to walk because of leg muscle fatigue, their productivity diminishes. If they also have a first heart attack as a consequence of their atherosclerotic disease, a preventable moment is lost.

Atherosclerotic peripheral artery disease (PAD) is one of the most prevalent, morbid, and mortal diseases. Globally, it affects more than 200 million people. It is associated with a high fatality rate due to cardiovascular ischemic events.

There are at least 4 key new insights that serve as major calls to action:

- 1) The contribution of key modifiable factors for the etiology of PAD—smoking, hypertension, and dyslipidemia. PAD is preventable.
- 2) It is a myth that PAD is a disease of the aged and is confined to high-income countries.
- 3) The supposition that PAD is more common in men than in women is inaccurate.
- 4) As communicable diseases decrease, the atherosclerotic syndromes become increasingly critical factors affecting public health.

Surgery—late stage leg revascularization cannot, in isolation, represent a sustainable strategy to decrease prevalence, morbidity, amputation rates, or mortality related to PAD.

In the USA, about 150 000 ischemic amputations are estimated to occur annually.

PAD is more common in low-income countries, and is increasing.

Lancet October 19, 2013;382: 1312-13 Commentary, first author Alan T Hirsch, University of Minnesota Medical School.

The literature I review focuses mainly on atherosclerotic heart disease and stroke. We may forget that peripheral arterial disease is also common and disabling.

Fortunately, the same interventions that protect against atherosclerotic heart and brain disease also protect the peripheral arteries.

10-6 FDA TIGHTENS INDICATIONS FOR USING LONG-ACTING AND EXTENDED-RELEASE OPIOIDS: Comment

In an effort to help curb the ongoing epidemic of prescription opioid abuse and overdoses, the FDA is tightening the indications for long-acting and extended-release opioids and is requiring drug manufacturers to conduct long-term post-marketing studies.

There was a 300% increase in prescription of opioid pain medications between 1999 and 2010. During this period, the number of pain-killer overdose deaths among women increased five-fold, and increased 3.6 fold among men. In 2010 alone, more than 15 000 US deaths were attributed to drug overdoses—nearly 2/3 due to opioids.

Calls for tighter restrictions: In July 2012, Physicians for Responsible Opioid Prescribing petitioned the FDA to change the labeling for opioids to curb abuse and limit indications for these drugs. The group argued that the drugs' indications were overly broad and not consistent with the evidence base, and may have been facilitated by marketing for broader use than was appropriate. They also argued that the FDA should drop moderate chronic non-cancer pain as an indication, set a maximum daily dose, and add a maximum duration of use of 90 days.

In March, The Drug Enforcement Agency (DEA) endorsed the idea of more limited indications for use of these drugs, and labeling revisions, to help mitigate the adverse impact on public health.

New labels, Long-term studies: The FDA is now requiring changes in the labels of all long-acting and extended-release opioids pain medications. The labels will specify that these medications are indicated only when the patient has severe enough pain to require daily and around-the-clock long-term opioid therapy. The new labels will also caution that there is a risk of addiction, abuse, misuse, overdose, and death, even at recommended doses. The labels will note that these drugs should be reserved for patients who cannot tolerate or get adequate relief from other pain treatments. Long-acting and extended-release opioids should not be given for “as needed use”. They should be reserved for patients without an alternative.

The new labels will carry a boxed warning about the risk of neonatal abstinence syndrome among infants born of mothers taking opioids.

Marketers of these drugs are being required to conduct long-term studies to assess the risks associated with their products for extended periods, and to provide information about their adverse effects.

Most opioid prescribing is for non-cancer pain—fibromyalgia, low back pain, and chronic headache, for which they are not appropriate.

The FDA did not make changes to labels of intermediate-acting opioids (hydrocodone and oxycodone), which are among the most prescribed drugs in the US. The FDA is focusing on extended-release and long-acting opioids because the agency believes that they play a disproportionate role in overdose and abuse.

The FDA would like to encourage physicians and patients to more thoroughly discuss benefits and risks of long-acting and extended-release opioids. Physicians and patients need to talk about the patient's individual needs to make sure the patient requires these opioid products to live and function better.

JAMA October 2, 2013;310:1547-48 “Medical News and Perspective” by Bridger M Kuehn, JAMA Staff.

